CLAIMS

We claim:

1. A method for using high affinity TCRs to identify ligands comprising:
labeling high affinity TCRs;
contacting said labeled TCRs with ligands;
identifying the ligand with which the labeled TCR is bound.

2. The method of claim 1, wherein said label is selected from the group consisting of:
fluorescent compounds, chemiluminescent compounds, radioisotopes and chromophores.

3. The method of claim 1, wherein said ligands are peptide/MHC ligands.

4. A method of using high affinity TCRs to bind to a selected peptide/MHC ligand comprising:
labeling said high affinity TCRs with a label that binds to the selected peptide/MHC ligand;
contacting said labeled high affinity TCRs with cells containing MHC molecules.

5. The method of claim 4, wherein said label is selected from the group consisting of:
fluorescent compounds, chemiluminescent compounds, radioisotopes and chromophores.

6. A method for using high affinity TCRs as diagnostic probes for specific peptide/MHC molecules on surfaces of cells comprising:
labeling high affinity TCRs with a label that binds to specific peptide/MHC ligands;
contacting said TCRs with cells;
detecting said label.

7. A method for using high affinity TCRs that bind to pMHCs for diagnostic tests comprising:
labeling the high affinity TCR with a detectable label;
contacting said high affinity TCR with cells;
detecting the label.

8. The method of claim 7, wherein the number of labels present is detected.

9. The method of claim 7, wherein the location of the labels is detected in an organism.

10. The method of claim 7, wherein said label binds to specific peptide/MHC ligands, whereby cells that express specific peptide/MHC ligands are targeted.

11. The method for blocking autoimmune destruction of cells comprising:
contacting TCRs with high affinity for the site recognized by the T lymphocytes on the surface of a target cell with cells, whereby the autoimmune destruction of cells is blocked.

12. The method for using high affinity TCRs to treat disease comprising:
coupling a TCR having a high affinity for a neoplastic cell surface marker with a therapeutic compound; and
contacting said TCR with cells.

13. A method of using high affinity TCRs to inactivate pathogens comprising:
binding a molecule which is toxic to the pathogen to the high affinity TCR; and
contacting said TCR with cells that express said pathogen.

14. The method of claim 13, wherein said pathogen is selected from the group consisting of: virus, bacteria and protozoa.

15. Soluble T cell receptors (TCRs) having higher affinity for a ligand than wild type TCRs.

16. The soluble high affinity TCRs of claim 15, wherein said ligand is a peptide/MHC ligand.

17. The soluble high affinity TCRs of claim 15, wherein said high affinity TCR is made by the method comprising: mutagenizing a TCR to create mutant TCR coding sequences; transforming DNA comprising the mutant TCR coding sequences for mutant TCRs into yeast cells; inducing expression of the mutant TCR coding sequences such that the mutant TCRs are displayed on the surface of yeast cells; contacting the yeast cells with a fluorescent label which binds to the peptide/MHC ligand to produce selected yeast cells; and isolating the yeast cells showing the highest fluorescence.

18. The soluble high affinity TCRs of claim 15 isolated by yeast display.

19. A DNA library comprising nucleic acids encoding soluble high affinity TCRs, wherein said TCRs are made by the method of mutagenizing a TCR to create mutant TCR coding sequences; transforming DNA comprising the mutant TCR coding sequences for mutant TCRs into yeast cells; inducing expression of the mutant TCR coding sequences such that the mutant TCRs are displayed on the surface of yeast cells; contacting the yeast cells with a fluorescent label which binds to the peptide/MHC ligand to produce selected yeast cells; and isolating the yeast cells showing the highest fluorescence.

20. A library of T cell receptor proteins displayed on the surface of yeast cells which have higher affinity for the peptide/MHC ligand than the wild type T cell receptor protein, wherein said library is formed by mutagenizing a T cell receptor protein coding sequence to generate a variegated population of mutants of the T cell receptor protein coding sequence; transforming the T cell receptor mutant coding sequence into yeast cells; inducing expression of the T cell receptor mutant coding sequence on the surface of yeast

cells; and selecting those cells expressing T cell receptor mutants that have higher affinity for the peptide/MHC ligand than the wild type T cell receptor protein.

~~20.~~ 21. A method for cloning the gene for a high affinity TCR mutant into a system that allows expression of the mutant on the surface of T cells comprising:
mutating TCRs to create high affinity TCR mutants;
cloning said TCR mutants into a vector;
transfecting the vector into T cells;
expressing the high affinity TCR mutant on the surface of T cells.

~~21.~~ 22. The method of claim 20, further comprising:
selecting those T cells that are activated by a peptide/MHC ligand more than the wild type.

~~22.~~ 23. The method of claim 20, wherein the transfected/infected T cells are used for recognition of selected peptide-bearing MHC cells.

~~23.~~ 24. T cells made by the method of claim 20.

add A1

add B4